



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/316,570	12/21/2005	Karl-Georg Schmidt	930008-2206	2127

20999 7590 11/28/2016
FROMMER LAWRENCE & HAUG
745 FIFTH AVENUE- 10TH FL.
NEW YORK, NY 10151

EXAMINER

ANTHOPOLOS, PETER

ART UNIT	PAPER NUMBER
----------	--------------

1611

NOTIFICATION DATE	DELIVERY MODE
-------------------	---------------

11/28/2016

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

prosecutiondocketing@flhlaw.com

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte KARL-GEORG SCHMIDT

Appeal 2014-002984
Application 11/316,570
Technology Center 1600

Before MELANIE L. McCOLLUM, ULRIKE W. JENKS, and
TAWEN CHANG, *Administrative Patent Judges*.

JENKS, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134(a) involving claims to a method of treating open-angle glaucoma with flupirtine. The Examiner rejects the claims as obvious. We have jurisdiction under 35 U.S.C. § 6(b).

We AFFIRM.

STATEMENT OF THE CASE

Claims 13, 24, and 29 are on appeal, and can be found in the Claims Appendix of the Appeal Brief. Claim 13 is representative of the claims on appeal, and reads as follows:

13. A method of treating human open-angle glaucoma, which comprises administering a therapeutically effective amount of a composition comprising flupirtine in capsule form to a patient in need thereof.

Appellant seeks review of the Examiner's rejection of the claims 13, 24, and 29 under 35 U.S.C. § 103(a) as unpatentable over Osborne¹ in view of Kerrigan² and Rote Liste³.

The issue is: Does the preponderance of evidence of record support the Examiner's conclusion that the claims are obvious based on the combined teachings of the references?

Findings of Fact

We adopt the Examiner's findings of fact and reasoning regarding the scope and content of the prior art (Final Act. 3–8; Ans. 3–8). For emphasis only we highlight the following:

FF1. "Ischemia is defined as an arrest of blood flow and consequent reduction of oxygen supply" (Osborne S106). "Ischemic neuronal death has traditionally been attributed to necrosis. Recently,

¹ Osborne et al., *Neuroprotection in Relation to Retinal Ischemia and Relevance to Glaucoma*, 43 Survey of Ophthalmology S102–S128 (1999) ("Osborne").

² Kerrigan et al., *TUNEL-Positive Ganglion Cells in Human Primary Open-angle Glaucoma*, 115 Arch Ophthalmol. 1031-1035 (1997).

³ Rote Liste® 05 042 (2002).

morphologic studies have characterized two distinct types of cell death: necrosis and apoptosis” (*id.* at S108).

FF2. Osborne teaches that “[r]ecent reports indicate that apoptosis is a cause of ganglion cell death in both primary open-angle glaucoma and AION [anterior ischemic optic neuropathy]” (*id.* at S107).

FF3. Osborne teaches that “ischemia-induced insults to the retina in vivo are ameliorated by MK-801, dextromethorphan, flupirtine, and memantine” (*id.* at S115).

FF4. As noted by the Examiner, Osborne “identifies flupirtine as a pharmaceutical that (1) maintains energy supply to the *retina*, (2) *inhibits* NMDA receptor *activation*, and (3) prevents *apoptotic* cell death” (Ans. 4 (citing Osborne S117, Table 7)).

FF5. Osborne teaches:

[D]rugs that can reduce NMDA-receptor activity by acting more indirectly on the modulatory redox site of the NMDA receptor may be more useful for human use. Present evidence suggests that flupirtine acts in this way, functioning as an oxidizing agent and thereby suppressing or facilitating channel opening on activation of the NMDA receptor. This provides an explanation as to why flupirtine has already been used clinically for other purposes without apparent side effects. The nontoxic effect of flupirtine, its effectiveness as a NMDA antagonist, and *its ability to blunt insults that lead to necrotic or apoptotic injury make flupirtine a possible drug for use in the treatment of glaucoma.*

(Osborne S118 (emphasis added).)

FF6. Kerrigan teaches that “[a]poptosis seems to be a mechanism of cell death in human eyes with primary open-angle glaucoma” (Kerrigan, Abstract; Final Act. 5). “There are potential therapeutic approaches to

block cell death by interfering with the apoptotic pathway” (Kerrigan, 1035; Final Act. 5).

FF7. The Examiner finds that “Rote Liste® 2002 teaches that *flupirtine* is commercially available in capsule form (see Entry No. 05 042). It is worth noting that *kapseln* is the German word for capsule” (Final Act. 5).

Principle of Law

“The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.” *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 416 (2007). As expressly recognized in *KSR*, any art recognized need or problem can provide a reason for combining claim elements. *Id.* at 416.

Analysis

Appellant contends that “different types of glaucoma share neither common therapeutic characteristics nor common clinical appearances with the instantly-claimed open-angle glaucoma” (Br. 3).

We are not persuaded by Appellant’s contention. We agree with the Examiner’s fact finding, statement of the rejection and responses to Appellant’s arguments as set forth in the Answer and Final Action. We find that the Examiner has provided evidence to support a prima facie case of obviousness for applying flupirtine to prevent apoptotic cell death associated with diseases of the eye including open angle glaucoma.

To summarize, Osborne discloses that the “nontoxic effect of flupirtine, its effectiveness as a NMDA antagonist, and its ability to blunt insults that lead to necrotic or apoptotic injury make flupirtine a possible drug for use in the treatment of glaucoma” (FF5). In addition, Osborne

“identifies flupirtine as a pharmaceutical that . . . prevents *apoptotic* cell death” (FF4). Kerrigan teaches that “[a]poptosis seems to be a mechanism of cell death in human eyes with primary open-angle glaucoma” and that “[t]here are potential therapeutic approaches to block cell death by interfering with the apoptotic pathway” (FF6; *see also* FF2). Based on these findings, the Examiner concludes that the combination of references would have motivated the ordinary artisan to “administer[] capsules comprising flupirtine (an inhibitor of apoptosis) to a patient suffering from primary open-angle glaucoma, in an effort to treat primary open-angle glaucoma by inhibiting apoptosis of retinal ganglion cells” (Final Act. 5–6; *see* FF1–FF7). We find no error with the Examiner’s rationale.

Appellant contends that in “examining Osborne in its entirety, it clearly pertains to prevention of ganglion cell or retinal neuron death, which is induced by retinal ischemia” (Br. 4). However, “open-angle glaucoma, unlike other types of glaucoma, does not show any signs of ischemia” (*id.*). “The minimal increase in intra-ocular pressure associated with **open-angle glaucoma** is insufficient to cause any impediment to the drainage of fluid in the eye, and therefore causes **no reduction in blood supply, and therefore no ischemia**” (*id.* at 3).

We are not persuaded. As the Examiner explains, Kerrigan suggests that a therapeutic approach is to inhibit apoptosis regardless of the reason for initiating programmed cell death (Ans. 8; FF6). Osborne teaches that flupirtine is a drug that prevents apoptotic death and is suggested for treatment in glaucoma based on the prevention of apoptosis (FF1–FF6). The test for obviousness is what the combined teachings of the references as a whole would have suggested to those of ordinary skill in the art. *In re*

Keller, 642 F.2d 413, 425 (CCPA 1981). Here, both references suggest the application of apoptosis inhibitors to prevent programmed cell death in cells of the eye; this is regardless of the mechanism that leads to the initiation of apoptosis.

According to the Schmidt Declaration,⁴ “open-angle glaucoma unlike other glaucomas slowly develops over years” (Schmidt Decl. 7). Specifically, “open angle glaucoma is very unusual when compared to other glaucoma types,” and that teachings from one type of glaucoma cannot be generalized to other types (*id.* at 8). “Most notably, open-angle glaucoma does not show any signs of ischemia, like other glaucomas” (*id.*)

As explained by the Examiner, the Schmidt Declaration is insufficient to overcome the prima facie case of obviousness because it “fails to address the teachings of Kerrigan et al., which are considered extremely relevant” (Ans. 7). Specifically, Kerrigan teaches that apoptosis is the mechanism of cell death in open-angle glaucoma and that there “are potential therapeutic approaches to block cell death by interfering with the apoptotic pathway” (FF6). We agree with the Examiner’s position, and further note that although open angle glaucoma may be unlike other glaucomas in its etiology, the therapy applied is common therapy as suggested by Ritch⁵ (*see* Schmidt Decl. 8). Specifically, Ritch suggests that for open angle glaucoma the treatment is “only common therapy, no specific therapy, medicinal and/or surgical decrease of pressure; although the pressure is not necessarily excessively increased” (Ritch 2). In other words, even if the underlying

⁴ Declaration under 35 U.S.S. § 1.132 by Karl-Georg Schmidt dated June 15, 2012 (“Schmidt Decl.”).

⁵ Ritch et al., *Glaucoma-different types of therapies*, The Glaucomas (1989).

pathological issues leading to the development of open-angle glaucoma are not known, the art suggests applying therapies used for other glaucoma types. This disclosure buttresses the Examiner's combination of Osborne, which teaches conventional therapies including the use of apoptosis inhibitors (FF5), and Kerrigan, which proposes apoptosis as the mechanism of cell death in open angle glaucoma and suggests a similar therapeutic approach (FF6).

We conclude that the evidence cited by the Examiner supports a prima facie case of obviousness with respect to claim 13, and Appellants have not provided sufficient evidence of secondary considerations that outweighs the evidence supporting the prima facie case. As Appellant does not argue the claims separately, claims 24 and 29 fall with claim 13. 37 C.F.R. § 41.37 (c)(1)(iv).

SUMMARY

We affirm the rejection of all claims.

TIME PERIOD FOR RESPONSE

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED